REMARKS

Applicants respectfully request reconsideration and withdrawal of the rejections of the claims, in view of the amendments and remarks presented herein.

Applicants have added no new matter by their amendments or new claims. Support will be found on pages 10 and 11 and 14-15 of the specification. Support is also provided on page 4, line 20 – page 9, line 27, and on pages 33, 38 – 40. See the following discussion for further explanation of Applicants' examples and figures.

Claim Rejections, 35 U.S.C. §112

The Examiner has rejected claims 1-4 under 35 U.S.C. §112, first paragraph. The Examiner alleges that the specification does not reasonably provide enablement for making and using methods for identification of therapeutic agents, which induce cell maturation or cell death by measuring levels of DM or extrachromosomal DNA.

Applicants respond that their amendments taken in context of the following remarks overcome this rejection.

Applicants' invention concerns a process by which extrachromosomal DNA of abnormal cells such as cancer cells can be eliminated by encapsulation of that DNA in micronuclei. The micronucleation causes development of a non-cancerous state for the cell. This non-cancerous state may be any of three possibilities including: 1) reversion of the cell to a normal state, 2) re-differentiation of the cell, and 3) cell death through apoptosis. Applicants have found that certain pharmaceutical agents will induce the encapsulation.

Applicants demonstrate these findings through their examples and figures. Figures 3A and B, the text at page 6, lines 5-17, and at page 33, line 14-page 34, line 18 of the specification provide experimental support for the feature that certain agents will increase micronucleation of extrachromosomal DNA (DM's). In particular, Figure 3A shows that agents such as aphidicolin, deferoxamine, guanazole, hydroxurea, cumarin, nicotinamide and DMSO increased the frequency of micronucleation formation in the test cells (the COLO 320DM cells). These agents are known to function as inhibitors of DNA replication, i.e., they are known anti-cancer agents. Figures 6A through 6C and the text at page 38, line 21 – page 40, line 14 of the specification show that the result of micronucleation is the conversion of the undifferentiated cell (the

neoplastic cell) to a normal state. That normal state may be any of three possibilities, all of which eliminate the threat of the undifferentiated character of the cell: a reversion, a differentiation or apoptosis. Any of these states is possible as a result of the micronucleation.

For these reasons, Applicants submit that their claims as amended and their new claims overcome this §112 rejection. Applicants have demonstrated by experimental example that test cells having double minute DNA can be used to screen for therapeutic agents that will cause neoplastic cells to convert. The screen assay may be either an observation of an increased rate of micronucleation or a conversion of the undifferentiated test cell to a normal state. Applicants respectfully request withdrawal of this rejection.

Claim Rejections, 35 U.S.C. §102

The Examiner rejected claims 1 and 4 under 35 U.S.C. § 102(b) as being anticipated by Tometsko (U.S. Patent 5,229,265; published July 20, 1993); and under 35 U.S.C. § 102(e) as being anticipated by Dertinger et al. (U.S. Patent 5,858,667; published January 12, 1999; filed September 6, 1996).

Applicants respond that both Tometsko and Dertinger provide assays for determining whether a compound **produces** DM's. The present invention provides an assay for determining whether a compound will **stop** the inheritance of DM's through a mechanism of micronucleation. The presently claimed assay involves a determination of whether an agent will **destroy** cells with DM's.

Said another way, the assays described by Tometsko and Dertinger will determine whether a chemical compound will cause a form of cancer indicated by the production of DM's. These assays are tests for carcinogens. In contrast, the presently claimed method will determine whether a chemical compound will cause reversion, differentiation or death of cancerous cells containing DM's. This method is a test for anticancer compounds.

For these reasons, Applicants submit that Tometsko and Dertinger do not anticipate or suggest the present claims. Applicants respectfully request withdrawal of this rejection.

CONCLUSION

Applicants respectfully submit that claims 1-9 are in condition for allowance. Reconsideration and an early allowance are respectfully requested.

Respectfully submitted,

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner of Patents, Washington, D.C. 20231, on this 29th day of December, 2000.

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Name

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Signature